

Claims

1. A method of inducing apoptosis of PV negative p53 wild-type, p53 mutant- or p53 related gene positive cells comprising contacting those cells with a PV E2 protein or a functional portion or derivative thereof or supplying to the cells a DNA sequence encoding a PV E2 protein or a functional portion or derivative thereof whereby apoptosis is induced in the cells.
2. A method of killing cells infected with an oncogenic virus comprising contacting those cells with a PV E2 protein or a functional portion or derivative thereof or supplying to the cells a DNA sequence encoding a PV E2 protein or a functional portion or derivative thereof whereby the cells are killed.
3. A method of killing PV negative oncogenic cells or oncogenic precursor cells comprising contacting those cells with a PV E2 protein or a functional portion or derivative thereof or supplying to the cells a DNA sequence encoding a PV E2 protein or a functional portion or derivative thereof whereby the cells are killed.
4. A method of inducing apoptosis of PV negative or PV positive cells comprising contacting those cells with a PV E2 protein or a functional portion or derivative thereof and wild-type p53 protein or a functional portion or derivative thereof whereby apoptosis is induced in the cells.
5. A method of inducing apoptosis of oncogenic cells comprising contacting those cells with a PV E2 protein or a functional portion or derivative thereof and a wild-type p53 protein or a functional portion or derivative thereof whereby apoptosis is induced in the cells.
6. A method of inducing apoptosis of PV positive cervical cancer cells comprising contacting those cells with a PV E2 protein or a functional portion or derivative thereof and wild-type p53 protein or a functional portion or derivative thereof whereby apoptosis is induced in the cells.

204790.01407

7. A method of inducing apoptosis according to any one of claims 1 to 6 comprising contacting cells with a) PV E2 protein, and b) wildtype p53 protein and/or drugs or pharmaceutical compositions that induce wildtype p53 or wildtype p53 function in cells containing mutant p53.
8. A method of inducing apoptosis in HPV negative cells according to any one of claims 1 to 5 comprising contacting cells with a PV E2 protein and at least one agent that activates p53 function.
9. A method according to any preceding claim in which a substantial proportion of cells in a treated cell population are killed.
10. A method according to any one of claims 4 to 9 in which the cells are infected with HPV.
11. A method according to claim 10 in which the cells are transformed by HPV.
12. A method according to claim 10 or 11 in which the HPV is integrated in the cell genome.
13. A method according to claim 10, 11, or 12 in which the HPV is type 16 and/or 18.
14. A method according to any preceding claim in which the cells are mammalian cells.
15. A method according to claim 14 in which the cells are for example cervical, breast, lung, brain, colon, oesophagus, melanoma, osteosarcoma, skin, liver, head, carcinoma, and leukaemia cells.
16. A method according to claim 15 in which the cells are in a mammalian subject

2047990-01402

17. A method according to claim 15 or 16 in which the cells are human cells.
18. A method according to any one of claims 1, 2 or 9 to 17 in which the cells are oncogenic cells or precursors thereof.
19. A method according to any preceding claim in which the cells are virally infected.
20. A method according to claim 19 in which the cells are infected with an oncogenic virus or retrovirus.
21. A method according to claim 20 in which the oncogenic virus is an HPV, Hepatitis B, Herpesvirus B, Epstein-Barr virus or Human T cell lymphotropic virus type 1 or type 2.
22. A method according to claim 19 in which the cells are infected with HIV or HIV-related virus.
23. A method according to any preceding claim in which an immune response, preferably a mucosal response is induced in the cells or subject.
24. A method according to claim 23 in which the immune response is a mucosal response.
25. A method according to any preceding claim in which the cells over-express p53 or a related gene or a mutant thereof.
26. A method according to claim 25 in which the p53 related gene is p63 or p73.
27. A method according to any preceding claim in which the E2 derivative or functional portion binds DNA less well than wildtype E2.

2047990-01402

28. A method of treating cervical cancer comprising contacting cervical cells of a subject with E2 or a functional portion thereof or supplying to the cells a DNA sequence encoding a PV E2 protein or a functional portion thereof.
29. A method according to claim 28 in which the subject is human.
30. A method according to claim 28 or 29 including inducing an immunological response in a subject against PV.
31. A method according to claim 23, 25, 28, 29 or 30 in which E2 is fused to another protein or functional portion thereof which elicits an immune response.
32. A method according to claim 32 in which the other protein or portion thereof is tetanus toxoid fragment C.
33. A method according to any preceding claim in which a DNA sequence encoding a portion or derivative of E2 is used in which the portion or derivative is defective in DNA binding compared to wild type E2 .
34. A method according to any preceding claim in which the E2 protein or functional portion or derivative thereof is complexed with DNA.
35. A method according to any one of claims 1 to 34 in which the PVE2 derivative is a DNA binding-defective E2 derivative comprising an E2 amino acid sequence lacking C terminal portion(s) of a native E2 sequence.
36. A method according to claim 35 in which the PVE2 derivative is a DNA binding-defective E2 derivative according to claim 35 comprising an E2 sequence in which the last 86 amino acids of the native E2 protein are missing.

2047990.0140T

37. A method according to claim 35 or 36 in which the PVE2 derivative is a DNA binding-defective E2 derivative comprises an E2 sequence in which amino acids 296, 299 and 304 of the native E2 protein are missing.
38. A homodimer comprising a DNA binding-defective E2 derivative comprising an E2 amino acid sequence lacking C terminal portion(s) of a native E2 sequence; or a DNA binding-defective E2 derivative according to claim 35 comprising an E2 sequence in which the last 86 amino acids of the native E2 protein are missing; or a DNA binding-defective E2 derivative comprises an E2 sequence in which the amino acids 296, 299 and 304 of the native E2 protein are missing.
39. A heterodimer comprising a DNA binding-defective E2 derivative comprising an E2 amino acid sequence lacking C terminal portion(s) of a native E2 sequence; or a DNA binding-defective E2 derivative according to claim 35 comprising an E2 sequence in which the last 86 amino acids of the native E2 protein are missing; or a DNA binding-defective E2 derivative comprises an E2 sequence in which the amino acids 296, 299 and 304 of the native E2 protein are missing.
40. A vector comprising a modified E2 DNA sequence or at least a portion of an E2 sequence in which the E2 DNA sequence encodes an E2 derivative which can kill p53 positive cells, PV positive cells, cells infected with an oncogenic virus or oncogenic cells.
41. A vector according to claim 40 which encodes a polypeptide which will generate an immune response in a mammalian cell.
42. A vector according to claim 41 in which a mucosal response is generated.
43. A vector according to claim 40, 41, or 42 in which the E2 DNA sequence encodes an E2 derivative which can inhibit viral replication.

10047990.01.14.02

44. A vector according to claim 43 in which the derivative will inhibit replication of HPV.
45. A vector according to claim 40, 41, 42, 43 or 44 in which the E2 DNA sequence encodes an E2 derivative which is defective in binding DNA compared to wild type E2.
46. A nucleotide sequence encoding an E2 derivative for use in a method according to claim 36.
47. A nucleotide sequence according to claim 46 in which the sequence is a DNA or RNA sequence.

2047990.01402